

ferent molecules, such as different DNA molecules, are close to each other in mass. The use of alternating fields each with an intensity gradient, tends to sharpen resolution dramatically and allow unexpected resolution for molecules close to each other in mass. Another use is resolving a great number of bands in the same gel, an important consideration when eucaryotic DNA is being analyzed. Yet another use of the new kind of electrophoresis is to purify molecules such as enzymes, e.g., urokinase, myosins or hyaluronic acids so as to provide a purified sample which can serve as the basis for developing a way to produce the same or an equivalent molecule. As yet another use, the effect of various agents, such as drugs, can be assessed for their effect on chromosomes, nucleic acids and proteins because of the ability to separate such materials provided by the invention. As yet another example, polymers can be accurately and quickly analyzed for molecular weight distribution, branching, and other physical properties by use of the new kind of electrophoresis. As still another example, intact or cut human, animal or plant chromosomes can be analyzed using the new kind of electrophoresis.

It should be clear that the laboratory device discussed in connection with FIGS. 1-8, and the particular kinds of electric fields used thereby, and the insert molding device discussed in connection with FIG. 14, are only specific examples which are convenient for explaining certain principles of the invention. Numerous variations are possible and are within the scope of the invention. For example, a differently shaped electrophoresis chamber, or differently produced, distributed or varied electric fields can be used so long as the particles are acted on by electric fields varying with time so as to move them in overall directions generally transverse to at least two of the relevant, operationally significant fields. For example, the desired fields can be generated by differently shaped electrodes, by suitably excited coils or by other sources or combinations of different (in kind) sources, and the relevant field directions can be controlled by other means, such as without limitation, changing the net direction of the field or changing the electrode characteristics (e.g., potential). Similarly, the desired field gradient can be produced in any number of ways, such as by selecting an appropriate shape for the relevant electrodes, by maintaining different electrode portions at different potentials or by the interaction of two or more fields. Moreover, more than two fields can be used, so long as the net effect is at least to act in the desired manner on a particle first in one direction, then in another direction transverse to the first, etc., so as to move the particle in a third direction transverse to the first two.

It has been found desirable, in the above-described preferred exemplary embodiment of the new electrophoresis device, to have a number of discrete electrodes, and to interconnect them through devices (such as diodes) which allow current flow to each in only a selected direction. Moreover, it has been found desirable to have the wire electrodes extend along the interior sidewalls of the chamber vertically, or nearly so, because such electrodes make it particularly convenient to generate the desired electrical fields, and because with such electrodes when they are long enough in the vertical direction it is possible to have several gel layers on top of each other, each containing samples of particles, and to subject all of them to substantially identical

electric fields so as to carry out electrophoresis in all of them concurrently. To generate more complex fields, or to provide more freedom of choice in producing fields of selected characteristics, such as the fields E, E1 and E2 in FIGS. 4-6, each electrode (or at least electrode of a selected plurality of electrodes) can have its own, switchable, power supply connection such that each can be selectively maintained at any positive or negative electrical potential within a selected range (or at ground). In some cases, as few as three electrodes will suffice, and two of them can be connected (intermittently) to the same potential, so long as they cooperate with each other to produce at least two electrical fields which have the desired characteristics (i.e., being transverse to each other).

As one variation, the new kind of electrophoresis arrangement described above can make use of high frequency switching between transverse fields, e.g., at frequencies in the range from about 10^6 to about 10^9 Hz, superimposed on one or more steady, or more slowly switching fields such as the fields E, E1 and E2 discussed above. It is believed that the rapidly switching field or fields can help rotate (or orient) particles such as macromolecules in a desired manner while the steady or slowly switching field or fields can serve to move the particles in the desired overall direction. This arrangement of rapidly switching fields and steady or slowly switching fields can in fact use as few as two transverse fields, at least one of them having a steady or slowly switching intensity component and a rapidly switching intensity component superimposed thereon. For example, mutually transverse fields E1 and E2 as in FIG. 7 can be used, but at least one of the electrodes can have superimposed on the illustrated squarewave voltage waveform, a much higher frequency voltage waveform of a selected amplitude, such as at a frequency from about 10^6 to about 10^9 Hz.

What is claimed is:

1. A gel insert useful for electrophoretic separations which comprises a gel matrix consisting of a solidified agarose or acrylamide suitable for use in an electrophoretic method and entrapped within the gel matrix are lysed cells and macromolecules derived from the lysed cells.
2. A gel insert of claim 1, wherein the macromolecules are DNA.
3. A gel insert of claim 1, wherein the macromolecules are intact chromosomes.
4. A gel insert of claim 1, wherein the lysed cells are mammalian cells.
5. A method of preparing a gel insert of claim 1 which comprises suspending cells in a liquid agarose or acrylamide suitable for use in an electrophoretic method, allowing the agarose or acrylamide to form a gel matrix in which the suspended cells are entrapped, diffusing a cell lysing reagent into the gel matrix containing the suspended cells so as to lyse the cells, and yield lysed cells and macromolecules derived from the lysed cells entrapped in the gel matrix.
6. A method of claim 5, wherein the gel inserts are formed in a predetermined size and shape in a mold by adding the cells and the liquid to the mold in measured amounts.
7. A method of claim 6, wherein the addition of the cells and the liquid is automated.

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